Form PTO-1390	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER BONN-059
	TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371	U.S. APPLICATION NO. 09/936079

INTERNATIONAL APPLICATION NO. PCT/FR00/00580	INTERNATIONAL FILING DATE March 9, 2000	PRIORITY DATE CLAIMED March 9, 1999
TITLE OF INVENTION: PUMPING DEVICE FOR TRANSFERRING AT LEAST A FLUID INTO A CONSUMABLE		DATE: September 7, 2001

APPLICANT(S) FOR DO/EO/US
Bruno COLIN

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [XX] This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.

2. [ ] This a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.

3. [XX] This express request to begin national examination procedures (35 U.S.C. 371(f) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).

4. [XX] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. [XX] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [XX] has been transmitted by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).

6. [XX] A translation of the International Application into English (35 U.S.C. 371(c)(2)).

7. [XX] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C 371(c)(3))
   a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [XX] have not been made and will not be made.

8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).

9. [ ] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).

10. [ ] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. [XX] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.

12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

13. [XX] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.

14. [ ] A substitute specification.

15. [ ] A change of power of attorney and/or address letter.

16. [XX] Other items or information:

    a. WO 00/53320 (first page only)
    b. International Search Report (PCT/ISA/210)
    c. Written Opinion (PCT/IPEA/408)
    d. International Preliminary Examination Report (PCT/IPEA/409)

U.S. Application No. 09/936079	International Application No. PCT/FR00/00580	Attorney's Docket No. BONN-059

17. [XX] The following fees are submitted:	CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5)): Search Report has been prepared by the EPO or JPO. **$860.00**	860.00	
International preliminary examination fee paid to USPTO (37 CFR 1.482). . **$690.00**		
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) **$710.00**		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO . . . . . **$ 1000.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4). . . . . **$ 100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 860.00	
Surcharge of $130.00 for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	12 - 20	0	x $ 18.00	$
Indep.claims	1 - 3	0	x $ 80.00	$
Multiple dependent claim(s) (if applicable)			+ $270.00	$
			TOTAL OF ABOVE CALCULATIONS =	$ 860.00
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$
			SUB TOTAL =	$ 860.00
Processing fee $130.00 for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				$
			TOTAL NATIONAL FEE =	$ 860.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +				$
			TOTAL FEES ENCLOSED =	$ 860.00
			Amount to be: refunded	$
			charged	$

a. [XX] A Credit Card Payment Form in the amount of $ 860.00 to cover the above fee is attached.

b. [ ] Please charge my Deposit Account No. 50-1258 in the amount of $_____ to cover the above fees. Two copies of this sheet are enclosed.

c. [XX] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-1258 . Two copies of this sheet are enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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September 7, 2001
Date

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:

Bruno COLIN

Serial Number: New Patent Application

Filed: September 7, 2001

For: PUMPING DEVICE FOR TRANSFERRING AT LEAST A FLUID INTO A CONSUMABLE

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

September 7, 2001

Please amend this application, prior to calculation of the filing fee, as follows:

IN THE SPECIFICATION:

Page 1, between the title and the first heading, please insert the following:

This application is a U.S. National Stage of International application PCT/FR00/00580, filed March 9, 2000 and published on September 14, 2000 in the French Language.

IN THE CLAIMS:

Please cancel claims 1-12 without prejudice or disclaimer.

Please add new claims 13-24 as follows:

13. (New) A pumping device for transferring a fluid sample within a sealed consumable, the transfer being performed between at least one first compartment, said to be initial, and at least one second

compartment, said to be receiving, via a narrower section such as a transfer channel,

wherein the point of intersection between an initial compartment and the narrower section is located in the lower part, preferably at the lowermost point of this initial compartment, and

wherein the point of intersection between a receiving compartment and said narrower section is located in the upper part, preferably at the uppermost point of this initial compartment, and

wherein at least one of the initial and/or receiving compartments can be deformed in such a way that each deformation induces transfer of all or part of the sample.

14. (New) The device of claim 13, wherein the point of intersection between an initial compartment and the narrower section is in contact with the sample, and wherein the point of intersection between a receiving compartment and said narrower section is not in contact with said sample.

15. (New) The device of claim 13, wherein the initial compartment(s) is/are located vertically, substantially above the receiving compartment(s).

16. (New) The device of claim 13, wherein the point of intersection between an initial compartment and the narrower section is at a higher point than the point of intersection between a receiving compartment and said narrower section.

17. (New) The device of claim 13, wherein each compartment to be deformed includes at least one partition which can be deformed, such as a flexible film stuck onto at least one side of the consumable.

18. (New) The device of claim 13, wherein at least one strip runs down the entire length or part of the length of each narrowed section to promote drainage of the fluid sample.

19. (New) The device of claim 13, wherein at least one of the compartments is associated with a buffer supply.

20. (New) A method for pumping comprising deforming an initial compartment of the device of claim 13 at least once, for transferring all or part of the sample via the point of intersection located between the initial compartment and a narrower section located in the lower part, and preferably at the lowermost part, of this initial compartment, and via the point of

intersection between a receiving compartment and the narrower section located in the upper part, and preferably at the uppermost part, of this receiving compartment.

21. (New) The method of claim 20, wherein it consists in deforming at least one of the initial compartments to raise the pressure in the gas in this compartment in order to transfer all or part of the liquid contained in said liquid into at least one receiving compartment.

22. (New) The method of claim 20, wherein it consists in deforming at least one of the initial compartments to create a higher pressure than normal in the gas in this compartment in order to transfer all or part of the gas contained in said liquid into at least one receiving compartment.

23. (New) The method of claim 20, alternatively, it consists in:
- deforming at least one of the initial compartments to create higher pressure than normal in the gas in this compartment in order to transfer all or part of said liquid into at least one receiving compartment, and
- deforming at least one of the receiving compartments to create higher pressure than normal in the gas in this compartment in order

to transfer all or part of the gas contained in said liquid into at least one initial compartment.

24. (New) The method of claim 20, wherein the device is a card which can be used in an inclined or vertical position.

IN THE ABSTRACT:

Please replace the original abstract with the attached Substitute Abstract.

REMARKS

This Preliminary Amendment cancels claims 1-12, adds new claims 13-24, amends the specification and presents a new Abstract. The amendment to the specification inserts a reference to parent application PCT/FR00/00580 pursuant to 37 C.F.R. § 1.78. New claims 13-24 are based on the amended claims presented during International Preliminary Examination, and have been further amended by eliminating multiple dependencies and drawing reference numerals, and by otherwise conforming the claims to U.S. practice. The Substitute Abstract is based on the PCT Abstract. A version with markings to show changes made is attached as an Appendix. Claims 13-24 are pending.

An Information Disclosure Statement is attached.

It is not believed that any fee is required for entry and consideration of this Preliminary Amendment. Nevertheless, the Commissioner is authorized to charge our Deposit Account No. 50-1258 in the amount of any such required fee.

PATENT

Prompt and favorable examination of the application are earnestly requested.

Respectfully submitted,

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Enclosures:
- Appendix
- Abstract of the Disclosure
- Information Disclosure Statement

New National Stage Application
PRELIMINARY AMENDMENT

PATENT

APPENDIX

Version With Markings to Show Changes Made

IN THE SPECIFICATION:

The paragraph inserted between the title and the first heading on page 1 is new.

IN THE CLAIMS:

Claims 1-12 have been canceled.

Claims 130-024 are new.

IN THE ABSTRACT:

The Substitute Abstract is new.

ABSTRACT OF THE DISCLOSURE:

A pumping device (1) for transferring a fluid sample (2) into a sealed consumable (3), the transfer being performed between at least an initial compartment (4) and at least a receiving compartment (5) via a narrowed section such as a flow path (6). The point of intersection between an initial compartment (4) and the narrowed section is located in the lower part, and preferably at the lowest level, of the initial compartment (4). The point of intersection between the receiving compartment (5) and the narrowed section is located in the upper part, and preferably at the highest level, of the receiving compartment (5). At least one of the initial compartment (4) and/or receiving compartment (5) can be deformed, such that each deformation activates the transfer of all or a part of the sample (2). The invention is particularly applicable to microfluidic devices used in biology.

Pumping Device for Transferring at least a Fluid Into a Consumable

DESCRIPTION

This invention concerns a pumping device for transferring a fluid sample within a sealed consumable, the transfer being performed between at least one first compartment, said to be initial, and at least one second compartment, said to be receiving, via a narrower section such as a transfer channel. The invention also has for its object a method for implementing such a device.

The background art is given in document EP-A-0.381.501 which describes an apparatus for carrying out nucleic acid amplification using the Polymerase Chain Reaction (PCR), at the same time preventing dissemination of nucleic acid in the atmosphere. To this end, the apparatus is sealed and the transfer of biological fluids between different compartments therein is carried out by actuating a flexible compartment wall from the outside. This involves the use of a roller to compress the initial compartment a single time in order to drive the liquid out towards a receiving compartment.

Document WO-A-97/27324 describes a device with a similar configuration in that the transfer of liquids inside a sealed compartment is carried out by actuating a flexible compartment wall from the outside. The objective too is identical in that it applies to nucleic acid amplification using the PCR technology

without any risk of contamination since the compartment is sealed. It includes a pumping device to transfer the fluid sample into a sealed consumable, the transfer being carried out from at least one first compartment, said to be initial, and at least one second compartment, said to be receiving, via a narrower section such as a transfer channel. In addition, at least one of the initial and/or receiving compartments can be deformed in such a way that the deformation drives the transfer of all or part of the sample. Nevertheless, the position of the initial and receiving compartments is not important according to the applicant's invention, only the position of the points of intersection being important, more precisely "the point of intersection between an initial compartment and the narrower section is located in the lower part, preferably at the lowermost point of this initial compartment, and the point of intersection between the receiving compartment and said narrower section is located in the upper part, preferably at the uppermost point of this initial compartment". These two characteristics allow complete transfer of the liquid contained in the initial compartment to the receiving compartment under the influence of gravity. This is not the case with the above-mentioned document since the point of intersection with the feed chambers (which contain either structural elements for the amplification process or the polymerase enzyme) is not at the

lowermost point. What's more, the card dealt with in this international application is not used in a vertical position but in a horizontal position since it is specified that there is an upper side and a lower side, both of which are connected to one another by an edge. This background art document provides for the fact that a compartment can be deformed so that each deformation induces transfer of all or part of the sample, but this deformation is not due to deformation of the film alone but rather due to the presence of a cushion which has to be added to the film, a restriction which complicates the production of such a system.

According to document EP-A-0.705.978, the problem tackled concerns the precision of the volume being pumped. The solution to the problem is to precisely restrict the displacement of the membrane by virtue of the shape of the pump structure. This pump structure consists of a diaphragm which divides a cavity into two concave parts: an upper one (liquid) and a lower one (air or vacuum). Liquid can only enter and leave the upper concave part through a single channel (marked 41) which is located in the upper position.

This structure is completely different from that described in the applicant's invention, and the problem-solving aspect is also completely different since the objective of our invention is to

optimize the transfer of a liquid and prevent the formation of bubbles.

All these devices share a major disadvantage when it comes to the efficiency of transfer. Thus, none take into account the arrangement of the compartments with respect to either one another or to the transfer channels. It is thus possible that just one air bubble could inhibit or block transfer of a liquid from an initial compartment to a receiving compartment. This might result in interference with the amplification reaction and lead to inaccurate results.

This invention proposes a solution to this problem by positioning in an advantageous way, on the one hand the initial compartment(s) with respect to the receiving compartments and, on the other hand, the compartments with respect to the transfer channels.

To this end, this invention concerns a pumping device for transferring a fluid sample within a sealed consumable, the transfer being performed between at least one first compartment, said to be initial, and at least one second compartment, said to be receiving, via a narrower section such as a transfer channel, characterized in that the point of intersection between an initial compartment and the narrower section is located in the lower part, preferably at the lowermost point of this initial compartment, and

that the point of intersection between a receiving compartment and said narrower section is located in the upper part, preferably at the uppermost point of this initial compartment, and that at least one of the initial and/or receiving compartments can be deformed in such a way that each deformation actuates the transfer of the sample.

This narrower section may consist of either a channel, a channel system of a wide range of different dimensions (of varying length, diameter and cross-sectional area) or a simple bottleneck. The only requirement is that the cross-sectional area of the narrower section must be smaller than that of the initial or receiving compartment at the point of intersection with the compartment concerned.

According to a preferred embodiment, the point of intersection between an initial compartment and the narrower section is in contact with the sample, and the point of intersection between a receiving compartment and said narrower section is not in contact with said sample.

According to a modified embodiment, the initial compartment(s) are placed vertically, substantially above the receiving compartment(s).

The word "substantially" should be interpreted as meaning that the two compartments are not positioned one above the other with

respect to the vertical. The notions of verticality and horizontally in this application are always used in relation to the direction of the force of gravity. Nevertheless, it is always possible to imagine using some other form of force, e.g. by performing centrifugation in which case, these notions should be taken in relation to the direction of the centrifugal force experienced by the sealed consumable, in which case vertical would correspond to a plane containing the resultant of the centrifugal force and horizontal to a plane perpendicular to this resultant. Gravity can be bypassed using other forms of force such as the action of a magnetic field with ferrofluid transport systems, and the action of electric fields such as those that have been described for electric and hydrodynamic pumps (Richter et al., Sensors and Actuators, 29, p159-165, 1991). As for centrifugation, the direction of the vertical and the horizontal is defined in relation to the direction of the resultant of the force which induces the displacement. In this case, the objective of the force is to position the liquid at the intersection between the initial compartment and the narrower section.

According to a preferred embodiment, the point of intersection between an initial compartment and the narrower section is at a higher point than the point of intersection between a receiving compartment and said narrower section.

This higher point should be interpreted as being in a first horizontal plane which contains the above-mentioned first point of intersection, at a higher position than a second horizontal plane which contains the first above-mentioned point of intersection. Preferably, every compartment which can be deformed includes at least one partition which can be deformed, such as a flexible film stuck to at least one of the sides of the consumable.

The consumable is a card which is used in a vertical position or on a slope, preferably in a vertical position. If gravity is being used as described above, the slope is measured with respect to the angle between the card and the horizontal. This angle must be greater than 10° (advantageously greater than 45° and preferably equal to 90°, i.e. in a vertical position).

According to a modified embodiment, at least one strip runs down the entire length or part of the length of each narrowed section to promote drainage of the fluid sample.

According to another modified embodiment, at least one of the compartments is associated with a buffer supply.

Such a buffer supply is thoroughly described and protected in the patent application filed by the applicant on the same day as this invention and entitled: "Test sample card with improved filling". The contents of the description of this patent application are considered as being included in this invention.

This invention also concerns a pumping method which consists in deforming one of the above-described devices at least once. According to a first modified embodiment, this method consists in deforming at least one of the initial compartments to create higher pressure than normal in the gas in this compartment in order to transfer all or part of the liquid contained in said liquid into at least one receiving compartment.

According to a second modified embodiment, this method consists in deforming at least one of the receiving compartments to generate an overpressure in the gas in this compartment in order to transfer all or part of the gas contained in said liquid into at least one initial compartment

According to a third modified embodiment, the method involves a combination of the two above-mentioned techniques. Alternatively, it consists in:

- deforming at least one of the initial compartments to create higher pressure than normal in the gas in this compartment in order to transfer all or part of the liquid into at least one receiving compartment, and
- deforming at least one of the receiving compartments to create higher pressure than normal in the gas in this compartment in order to transfer all or part of the gas contained in said liquid into at least one initial compartment.

According to a fourth modified embodiment, in the case in which a buffer supply is associated with at least one of the initial or receiving compartments, the method consists in simultaneously deforming the initial or receiving compartment and the buffer supply. Thus, in the case of a test sample card with cavities covered with flexible film, when pressure is applied to the flexible film to reduce the volume in one of the compartments, it is also possible to simultaneously compress the associated buffer supply. Therefore, it is particularly useful to have a compartment and a buffer supply located on either side of the card, opposite one another, so that the pressure applied to both compartments is additive. Of course, every receptacle has to be covered by a flexible film which may be the same as long as said film accepts said card in sandwich configuration. Of course, this fourth embodiment can be combined with the other embodiments.

There are various different ways of compressing the compartment, e.g. a striker which can be switched between two different positions to exert a series of successive pressurizing operations on the compartment. The movement of such a striker might be controlled by an electric or pneumatic motor. This striker could be made of any kind of material, e.g. metal or plastic, as long as its mechanical strength is compatible with the pressure it is to exert on the compartment to be deformed.

Such a device can be used with consumables in the analysis of one or more different liquid samples to identify one or more analytes, using any method, be it a simple or complex method and be it based on one or more different reagents, depending on the chemical, physical or biological nature of the analyte being tested. The technical principles defined hereafter are not restricted to any single, specific analyte; the only required condition being that the analyte must either be dissolved or in suspension in the test sample. In particular, the test process being used can be performed on a homogenous, heterogeneous or mixed form.

One particular, non restricted mode of such a consumable, concerns biological tests for the detection and/or quantitative determination of one or more ligands, in which the assay involves one or more anti-ligands. The word ligand is taken to mean any biological species, e.g. an antigen, a fragment of an antigen, a peptide, an antibody, a fragment of an antibody, a hapten, a nucleic acid, a fragment of a nucleic acid, a hormone or a vitamin. One example of an application of the test methods concerns immunoassays, whatever their particulars and whether the assay is direct or based on competition. Another example of an application concerns the detection and/or quantitative determination of nucleic acids, including all operations required for such detection and/or

quantitation in any kind of sample containing the target nucleic acid species. Among such diverse operations, the following could be specified: lysis, fluidification, concentration, enzyme-mediated nucleic acid amplification, and detection modalities which include a hybridization step using, for example, a DNA chip or a labeled probe. Patent application WO-A-97/02357 stipulates the various stages involved in the case of nucleic acid analysis.

The notion of the sealed consumable is a particularly important one in the case in which an enzyme-mediated amplification reaction is being carried out in the consumable, because the contamination inherent to these reactions can be avoided by using such sealed consumables, and because it is particularly advantageous to have a simple method of displacing liquids such as the one described in this invention. The notion of the sealed consumable should be understood as meaning that the consumable is sealed during certain steps of the process, notably during the phase in which the fluids are displaced by pumping. Actually, a sample containing one or more ligands to be tested has to be introduced into a consumable in order to carry out the test for said ligands. Therefore, at this stage of the process, the consumable has to be open. Similarly, the whole consumable does not have to be sealed to achieve the purpose of the invention. The fluid part concerned by the pumping device could be isolated by,

for example, a valve system, with the rest open to the outside so that the necessary reagents can be introduced into the consumable for a reaction to take place at a later stage.

The accompanying drawings are given by way of example and are not to be taken as in any way limiting. They are intended to make the invention easier to understand.

Figure 1 shows a partial, longitudinal section through a pumping device for a sealed consumable, according to this invention, in the simplest embodiment possible with a single initial compartment and a single receiving compartment.

Figure 2 shows a partial, transverse section of the compartment of a pumping device according to Figure 1.

Figure 3 shows a partial, longitudinal section through a pumping device for a sealed consumable, according to this invention, in a more complex embodiment with a single initial compartment and three receiving compartments.

Figure 4 shows a longitudinal section of a sealed consumable which includes a pumping device according to this invention, in an embodiment which is substantially of the same degree of complexity as that in Figure 2 but with three key differences. Firstly, it has one initial compartment and five receiving compartments. Secondly, the receiving compartments have a particular configuration. And thirdly, the position of the initial

compartment with respect to the receiving compartments is different from that in the previous Figures.

Figure 5 shows a partial, longitudinal section through a pumping device for a sealed consumable, according to this invention, in a more complex embodiment with three initial compartments and three receiving compartments.

Finally, Figure 6 shows a partial, transverse section identical to that in Figure 2, but in which the flexible film of the pumping device is subjected to an external force which induces the pumping action.

This invention concerns a pumping device (1) which is clearly shown in Figures 1 to 5, and which is particularly well suited for the transfer of fluids – both liquids and gases – inside a sealed consumable (3).

It should first be noted that Figures 1, 2, 3 and 5 are all views of longitudinal sections through different embodiments of the pumping device (1), but that the grooves which would normally be present around the edge of said device (1) have been omitted in order to make the mechanism easier to understand. Therefore, it is important to appreciate that the elements which are represented (i.e. the initial compartments [4], the receiving compartments [5], and the narrower sections or channels [6]) are actually embedded into a consumable (3), as clearly shown in Figure 4.

Figure 1 shows a simple embodiment of this invention. It is characterized by the presence of a single first compartment said to be initial (4) located at the top, and a second compartment, said to be receiving (5) located below. Of course, both the shape and volume of these compartments (4 and 5) can be different from one another and from those represented in the figures. The two compartments (4 and 5) are connected to one another by a channel (6), the shape of which is specially conceived. Likewise, the volume of this channel (6) has to be matched to the size of the compartments and to their relative position with respect to one another. More details about this will be given later on.

It can be seen that the position of the points at which the channel (6) intersects the compartments meet certain specification. Thus, this point of intersection is found at the lowermost point of the initial compartment (4) and at the uppermost point of the receiving compartment (5).

As it can easily be seen, there is a fluid sample (2) present in the pumping device (1). This sample (2) is actually a liquid. The point of intersection between the channel (6) and the initial compartment (4) is therefore in contact with the sample (2) which, under the influence of gravity, falls to the bottom of said compartment (4). In contrast, the point of intersection between the channel (6) and compartment (5) is in contact with the air

contained in said compartment (5), the liquid (2) being present throughout the length of the channel (6). The fluid sample (2) is therefore only found at the bottom of compartment 5. Thus, as shown in Figure 1, there are successive phases of gas (air) alternating with liquid (the sample 2).

Part of the sealed consumable (3) containing the pumping device (1) is shown in Figure 2 which corresponds to a cross-section through A-A in Figure 1. It can be seen that it substantially concerns a card with cavities, said cavities being defined on one side by the material of the consumable (3) (e.g. plastic), and on the other side by a very thin, flexible partition (7). This partition might be made of polyethylene or any other material which can be easily deformed, including silicone, latex and polyimides.

The nature of the flexible film may vary according to the nature of the test card and of the fluids being tested, especially when compatibility is at issue. For example, TPX (polymethyl pentene copolymer) or BOPP (bi-oriented polypropylene) films are suitable for biological assays. These films can be fixed in place either using an adhesive, (with the adhesive applied to the film, e.g. a silicon-based adhesive) or by heat-sealing. An example of a BOPP adhesive is available from BioMérieux Inc. (St. Louis, MO, USA) (reference: 022004-2184).

In terms of production, the card is manufactured by the machining of special plastic material, e.g. impact polystyrene (reference: R540E from the Goodfellow company) which is compatible with the liquids being processed. For industrial-scale production, the card could be manufactured by precision molding, but any other manufacturing method (including those used in the semi-conductor industry as stipulated in patent application WO-A-97/02357) may be used for test card production.

Therefore, it is easy to understand how this pump inside a sealed consumable (3) works when simple pressure (F) is applied to a flexible film (7), as clearly shown in Figure 6. When said film (7) is compressed, the volume of the air in the initial compartment (4) will decrease and the liquid (2), being incompressible, will be driven along the channel (6) into the receiving compartment (5). Of course, in order to prime such a pumping device (1), the displacement of the flexible film (7) will have to be sufficient to transfer a greater volume of the liquid sample than the total volume of the channel (6).

Another condition essential for the proper functioning of the device is that there is a step at the point where the liquid reaches the intersection between the channels (6 or 8) and the receiving compartment (5). The liquid which falls down into

compartment (5) will not be able to return via the channels (6 or 8) when the pressure is released on the part which can be deformed.

By exerting successive actions of the flexible film (7), the whole fluid sample can be transferred from the initial compartment (4) to the receiving compartment (5).

It is also possible to imagine that this system is also only found in compartment 5 and that the pumping action is triggered by simply depressing a film (7) which is only present on this receiving compartment (5). In this case, the starting volume of the receiving compartment (5), once compressed, is reduced and air is transferred via channel (6) into the initial compartment (4). In the same way as above, it is important that enough air is driven out of the receiving compartment (5) to reach the initial compartment (4). To insure this, this volume of displaced air must be greater than the volume of the channel (6).

According to a final modified embodiment, it would also be possible to press alternately on the film (7) covering the initial compartment, and on the film (7) covering the receiving compartment in order to accelerate transfer by the pumping device (1).

As shown in Figure 3, another embodiment includes a single initial compartment (4) and three receiving compartments (5). To make this work, the channel (6) has a special configuration in that there exists a primary channel (8) for each compartment (4 or 5)

and an intermediate channel (9) connecting all the primary channels (8). Although this is not represented in the Figures, the shape of the various channels (e.g. 6, 8, 9, 10 and 11) must be matched to the different embodiments, in particular when the system includes a distribution function with numerous receiving compartments. Those skilled in the art will choose for each channel a shape that provides a balanced distribution, including by varying pressure losses. Elbows and narrower sections are ways of modulating this pressure loss and avoiding the preferential filling of one receiving compartment over another. In contrast, when different volumes are to be sent to different receiving compartments (for different reactions being conducted in the compartments), those skilled in the art can vary the shape of channels to achieve the desired filling profile.

The nature and dimensions of the channels will also be selected to insure the liquid-gas exchanges necessary for the proper functioning of the pumping device. For example, in the case of a liquid being transferred with the device in Figure 1, the cross-section of the narrow channel (6) will be matched to the viscosity of the liquid so that an air bubble can float back up. It is particularly advantageous to minimize the volume of the channel (6) compared with the volume of liquid to be transferred to cut down dead space, especially when the initial compartment is not

located above the receiving compartment(s) (with reference to gravity).

An appropriately configured system of valves can also be used to control filling of the receiving compartments, possibly in association with channel shape. Such valves could have different functions, e.g. a distribution-related function making it possible to direct the fluid in a particular way in order to be able to dispense with the distribution channel (11) in Figure 4, or an opening/closing function to isolate the whole card or a single compartment therein (like valve 15 in Figure 4).

Figure 5 is also a particular embodiment in which there are three initial compartments (4) and three receiving compartments (5). In this case, the structure of the narrower section or channel (6) is more complex since there is both a primary channel (8) for every compartment (4 and 5) as already seen in Figure 3, and also an intermediate channel (9) for every group of initial or receiving compartments (4 and 5). Preferably, the two intermediate channels (9) run parallel to one another. Between these two channels (9), there are other channels, said to be secondary (10). The number of secondary channels (10) is not in any way fixed – there may be just one or there may be many. In the embodiment shown in Figure 5, the two channels (10) are in fact arranged to insure better distribution of the liquid samples (2) being

transferred from the initial compartments (4) to the receiving compartments (5).

This type of reaction also necessitates precise quantitation of the volumes being transferred. This invention allows such controlled distribution. This function will be explained next.

In another embodiment which is not shown, it would also be possible to transfer the gas and use a liquid as the barrier between different gas samples.

Therefore, it should be understood that this invention can also be used with the roles of the gas and liquid reversed since every compartment is partially filled with both phases at the time of pumping. In this context, it is worth noting that, at the beginning of pumping, the initial compartment can be full of liquid and the receiving compartment full of gas. Similarly, it is also possible that said receiving compartment already contains at least one substance which might be a liquid and/or a solid. For example, the lining of the compartment could contain at least one reagent ready to be reacted with the transferred sample (2).

Figure 4 shows an embodiment which is substantially closer to a model which might be produced on an industrial scale. The device functions in substantially the same way as that shown in Figure 3 with a single initial compartment (4) and five receiving compartments (5).

There are also important differences between Figures 3 and 4. Thus, in Figure 4, it is evident that the initial compartment (4) is located below the receiving compartments (5). In fact, there are no restrictions on the arrangement of the various compartments (4 and 5) with respect to one another although the preferred use of such a device would be when the column of liquid (2) present in the initial compartment (4) helps transfer into the receiving compartments (5) through the influence of gravity. The embodiments in Figures 1, 2, 3 and 5 are therefore of particular interest. A second difference derives from the structure of the receiving compartments. At their top, these include an apparatus for bursting bubbles (13) (for which a patent application has also been filed by the applicant, as mentioned above). Still in the context of this other patent application, at the top of said apparatus (13) can be seen an opening (14) which provides a route of communication between said apparatus (13) and a buffer supply (the role of which is explained in detail in the other patent application). Such a buffer supply is present on the other side of the consumable (3) which is made in the shape of a card.

Another difference lies in the presence of an intake channel (12) via which the fluid sample (2) can be injected or transferred from another consumable or from another part of the same consumable (3), an embodiment which is not represented in this figure, the

sample (2) being thus transferred towards a distribution channel (11) located substantially in the middle of the card.

From this distribution channel (11), a number of primary channels (8) connect this channel (11) to all the compartments (4 and 5). Thus, it is possible to have a liquid (17) inside the initial compartment (4), this liquid (17) being non-reactive with the liquid sample (2) which was introduced. This liquid (17) is used to make it possible to act upon and push the sample (2) present in the distribution channel (11) towards the receiving channels (5) via the primary channels (8). It can also be seen from Figure 4 that the consumable (3) is provided with an outlet channel (16). This channel (16) makes it possible to remove a sample (2) contained in at least one of the receiving compartments (5). The valves (15) located in the outlet channel system (16) are used to select the receiving compartment(s) (5) which is (are) to be emptied. It can also be seen that there is a valve (15) on the intake channel (12).

The total volume of liquid which can be transferred by this device can vary from 0.5 to 5000 microliters, advantageously between 2 and 2000 microliters and preferably between 5 and 1000 microliters. If a large volume is to be transferred (e.g. over 500 microliters), an embodiment based on successive pressurizations is to be preferred to transfer fractions of the liquid, each of

between 5 and 100 microliters (µl) in volume. The volume of the initial compartment covers the same range (or perhaps a substantially greater range) as the total transferred volume. By way of example, in the embodiment in Figure 4, the volume of compartment (4) is of between 2 and 5 ml for a transfer of between 250 and 500 µl of liquid. The total volume for the fluid part represented by channel (8) which connects the initial compartment (4) and the receiving compartments (5) is 120 ml (i.e. 20 µl for the part of the canal [8] connecting the receiving compartment [5] and the distribution channel [11], and five times 20 µl for the part of the channel [8] connecting the distribution channel [11] and the receiving compartments [5]). In this example, channel 8 has a semi-circular cross-section with a diameter of 0.5 mm.

The applicant has already filed a patent application relating to the transfer from another consumable (3) as well as the valves (15) on September 8, 1998 under application number FR98/11383, and entitled: "A device in which reactions can be performed, a transfer system between devices and a method for using such a system ". The contents of the description of this patent application are considered as being included in this invention.

Although intake channels (12), outlet channels (16) and valves (15) are not described with reference to Figures 1, 2, 3, 5 and 6,

it is, of course, evident that these pumping devices (1) are fitted with them to insure proper functioning, even if they are not shown in the figures.

REFERENCES

1. Pumping device
2. Fluid sample
3. Sealed consumable
4. First compartment said to be initial
5. Second compartment said to be receiving
6. Narrower section or channel
7. Partition which can be deformed or flexible film
8. Primary channel
9. Intermediate channel
10. Secondary channel
11. Distribution channel
12. Intake channel in the consumable (3)
13. Bubble-bursting system
14. Opening affording communication between the apparatus (13) and a buffer supply
15. Valve
16. Outlet channel from the consumable (3)
17. Non-reactive liquid to transmit action to the liquid sample (2)

F. External force applying pressure to the film 7

CLAIMS

1. A pumping device (1) for transferring a fluid sample (2) within a sealed consumable (3), the transfer being performed between at least one first compartment, said to be initial (4), and at least one second compartment, said to be receiving (5), via a narrower section such as a transfer channel (6), characterized in that the point of intersection between an initial compartment (4) and the narrower section is located in the lower part, preferably at the lowermost point of this initial compartment (4), in that the point of intersection between a receiving compartment (5) and said narrower section is located in the upper part, preferably at the uppermost point of this initial compartment (5), and in that at least one of the initial and/or receiving compartments (4 and/or 5) can be deformed in such a way that each deformation induces transfer of all or part of the sample (2).

2. The device, according to claim 1, characterized in that the point of intersection between an initial compartment and the narrower section is in contact with the sample, and in that the point of intersection between a receiving compartment and said narrower section is not in contact with said sample.

3. The device, according to either of claims 1 or 2, characterized in that the initial compartment(s) (4) is/are located vertically, substantially above the receiving compartment(s) (5).

4. The device, according to any of claims 1 through 3, characterized in that the point of intersection between an initial compartment (4) and the narrower section (6) is at a higher point than the point of intersection between a receiving compartment (5) and said narrower section (6).

5. The device, according to any of claims 1 through 4, characterized in that each compartment (4 or 5) to be deformed includes at least one partition which can be deformed, such as a flexible film (7) stuck onto at least one side of the consumable (1).

6. The device, according to any of claims 1 through 5, characterized in that the consumable is a card which is to be used in a vertical position or on a slope.

7. The device, according to any of claims 1 through 6, characterized in that at least one strip runs down the entire

length or part of the length of each narrowed section to promote drainage of the fluid sample.

8. The device, according to any of claims 1 through 7, characterized in that at least one of the compartments is associated with a buffer supply.

9. A method for pumping, characterized in that it consists in deforming a device according to any of claims 1 through 8 at least once.

10. The method, according to claim 9, characterized in that it consists in deforming at least one of the initial compartments to raise the pressure in the gas in this compartment in order to transfer all or part of the liquid contained in said liquid into at least one receiving compartment.

11. The method, according to claim 9, characterized in that it consists in deforming at least one of the initial compartments to create a higher pressure than normal in the gas in this compartment in order to transfer all or part of the gas contained in said liquid into at least one receiving compartment.

12. The method, according to claim 9, characterized in that, alternatively, it consists in:

- deforming at least one of the initial compartments to create higher pressure than normal in the gas in this compartment in order to transfer all or part of said liquid into at least one receiving compartment, and
- deforming at least one of the initial compartments to create higher pressure than normal in the gas in this compartment in order to transfer all or part of the gas contained in said liquid into at least one receiving compartment.

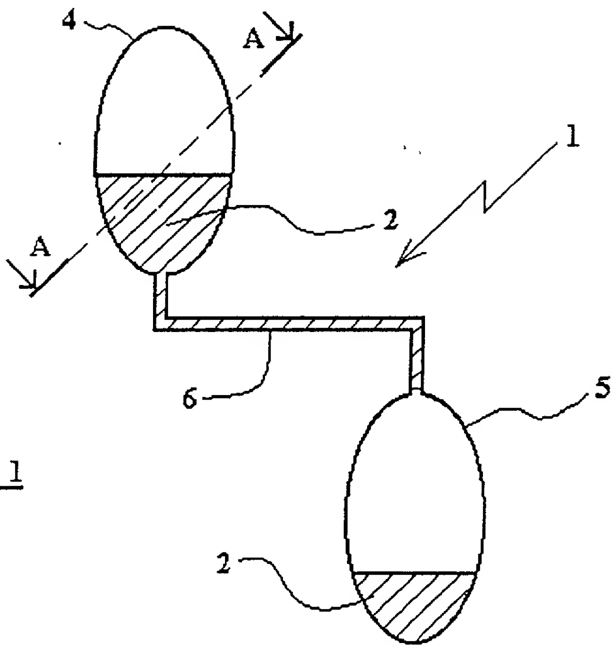


Fig. 1

Section A-A

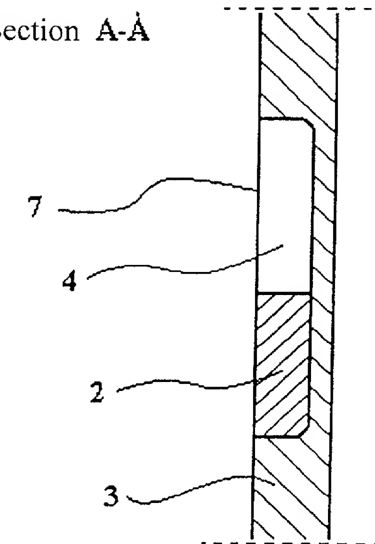
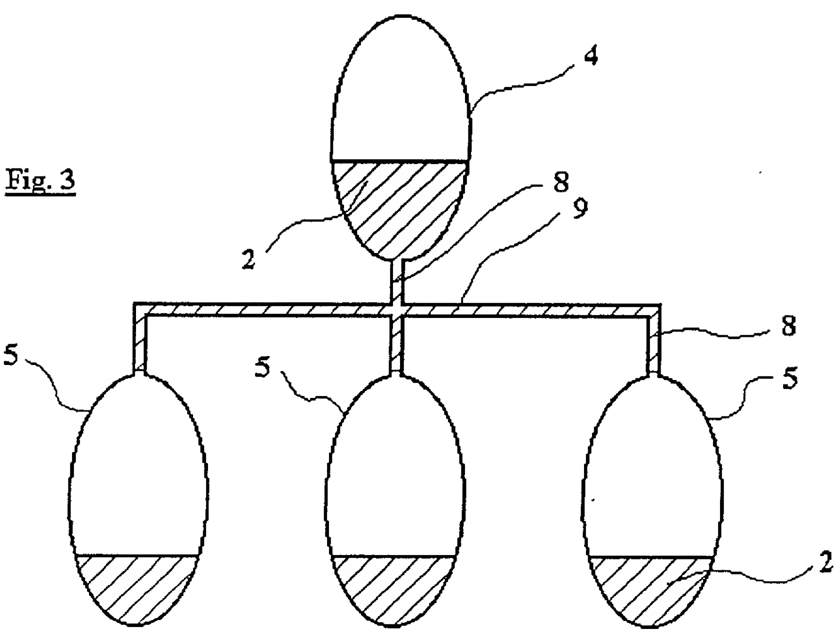


Fig. 2

Fig. 3



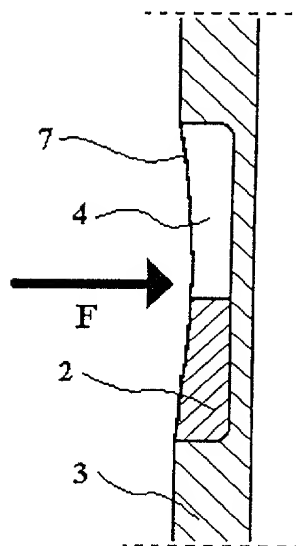


Fig. 6

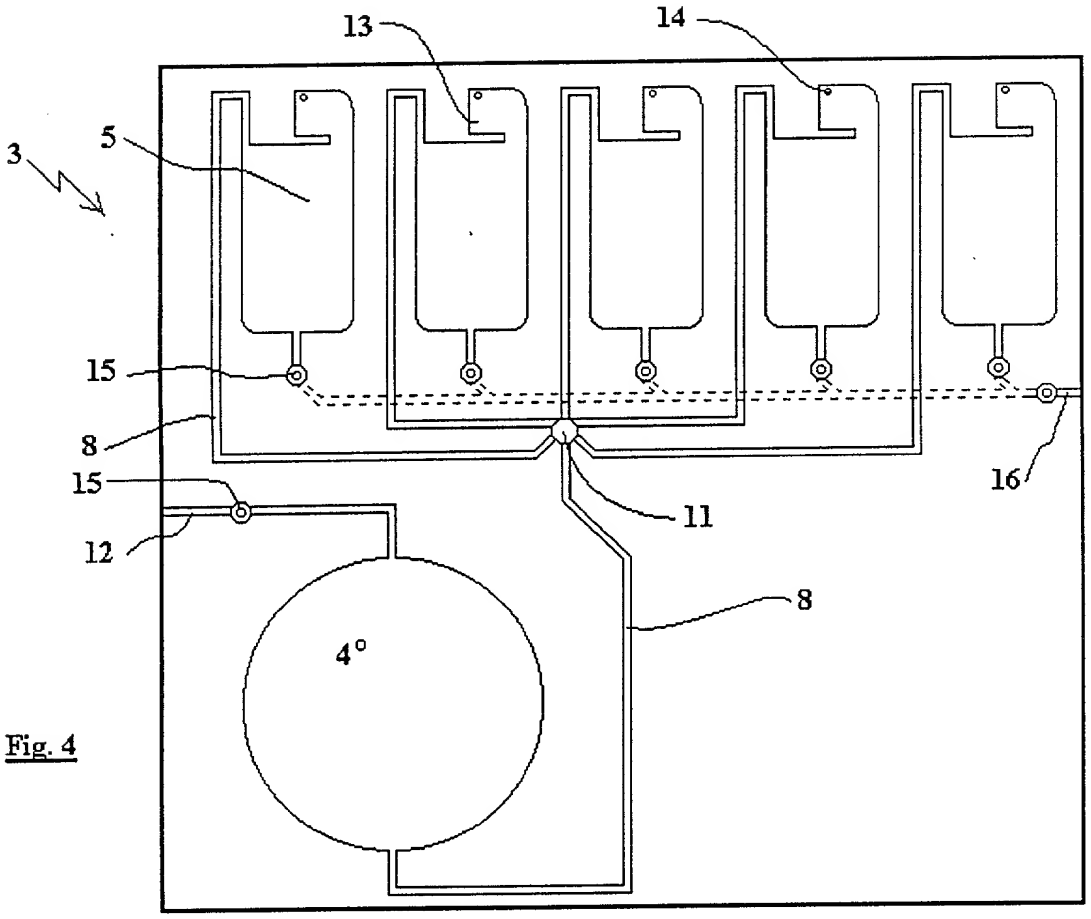


Fig. 4

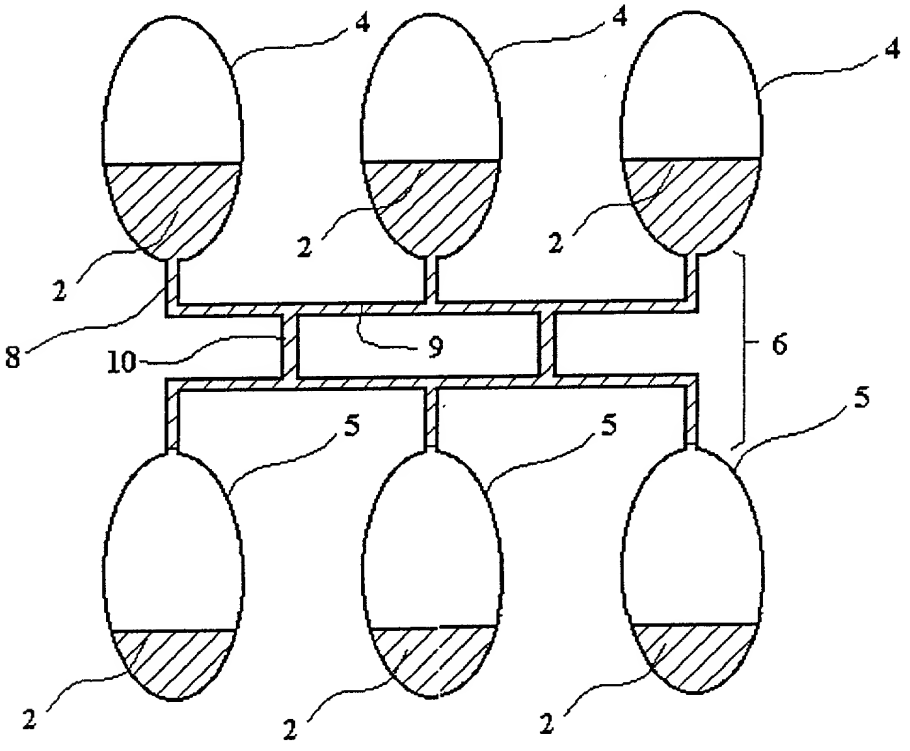


Fig. 5

Docket No. BONN-059

Declaration For U.S. Patent Application

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled (INSERT TITLE) Pumping device for transferring at least a fluid into a consumable

the specification of which

(Check one of 1, 2, or 3.)

1. __ is attached hereto.
2. XX was filed on March , 9, 2000 as International PCT Application Serial No. PCT/FR00/00580 and was amended on March 14, 2001 (if applicable).
3. __ was filed on _____ as U.S. Application Serial No. _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claim(s), as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application for which priority is claimed:

(List prior foreign applications.)	(Number)	(Country)	(Day/Month/Year Filed)	Priority Claimed
	99/03031	FRANCE	March 9, 1999	X Yes ___ No
				___ Yes ___ No

___ See attached list for additional prior foreign applications

I hereby claim the benefit under Title 35, United States Code, §120, of any United States application listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56, which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.)	(Filing Date)	(Status)
(Application Serial No.)	(Filing Date)	(Status)

I hereby appoint as principal attorney James C. Lydon, Reg. No. 30,082.

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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